

1. Susan A. Slaughaupt and James S. Acierno, Jr. are citizens of the United States of America. Ehud Goldin is a citizen of Israel. Mei Sun is a citizen of China. Each of us is more than twenty-one years of age.

2. We are the inventors of the above-identified application.

3. We reaffirm our duty of candor and good faith in dealing with the Office, including the duty to disclose to the Office all information known to be material to the patentability of the invention as defined in 37 C.F.R. § 1.56.

4. We have read and are familiar with the instant application as it was filed in the U.S. Patent and Trademark Office.

5. We have read and are familiar with the publications by (i) Curtis et al. (Pub. No. US 2002/0035056 A1), which we understand has an effective filing date under 35 U.S.C. 119(e) of Apr. 07, 2000; and (ii) Lal et al. (Pub. No. US 2002/0182671 A1), which we understand has an effective filing date under 35 U.S.C. 119(e) of Aug. 17, 1999.

6. It is our understanding that, according to the Examiner, the amino acid sequence presented in SEQ ID NO: 3 of the instant application is identical to the amino acid sequence presented in SEQ ID NO: 2 of Curtis et al. and SEQ ID NO: 13 of Lal et al. It is further our understanding that the Examiner states that Curtis et al. and Lal et al. each present an isolated nucleic acid encoding a protein comprising the amino acid sequence presented in SEQ ID NO: 3 of the instant application, as well as a vector and host cell comprising that nucleic acid.

7. Prior to Aug. 17, 1999, the effective date of the Lal et al. publication, we conceived and reduced to practice the invention as described and claimed in claims 1, 5-7, 33-34, and 39 of the subject application.

8. The inventive work embodied in all claims of the subject application was carried out in its entirety in the United States of America.

9. As evidence that our reduction to practice antedates Lal et al., we refer to Exhibits 1 and 2, which collectively establish the conception and reduction to practice of our invention prior to Aug 17, 1999. The exhibits verify the isolation and possession of a nucleic acid encoding MCOLN1 prior to Aug. 17, 1999. Dates, along with privileged information, appearing in these documents have been redacted, but each document has a date before August 17, 1999.

10. Exhibit 1 establishes identification of MCOLN1 sequence, showing the receipt by Dr. Slaughaupt of two primers: (i) sts-T66288-R (5'-AGC TGC AGG CCT ACA TCG -3'); and (ii) sts-T66288-F (5'GGC AGT CAG GTC GAA TCA AT-3). As shown in Appendix A, the two primers are specific to the MCOLN1 gene, spanning the 1732-1883 bp region of the MCOLN1 cDNA sequence (SEQ ID NO: 3).

11. Exhibit 2 shows the identification and possession of a nucleic acid encoding a full-length MCOLN1 protein by presenting an EST alignment spanning the MCOLN1 gene. At least two notations are particularly relevant. First, this page shows a "2264 bp" annotation of T66288 following sequencing, indicating that T66288 encodes the entire MCOLN protein. Prior to our sequencing, the exact insert size of this construct was not known.

Second, this page also identifies the orientation of AI8166064, which is the corresponding GenBank accession number for IMAGE CLONE 2517653 (Appendix B). Paragraph [0185] of the specification states that we “sequenced the IMAGE clone 2517653.” This paragraph further describes our deduction and confirmation of the MG-2 (MCOLN) open-reading frame from this clone.

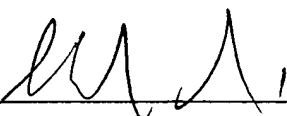
12. With the isolation and identification of the MCOLN1 coding region, we also achieved reduction to practice of an expression vector encoding the MCOLN1 protein prior to August 17, 1999. Appendix B reveals that IMAGE CLONE 2517653 (as presented in Exhibit 2) is inserted into the pBluescript SK+ vector. This common vector is widely recognized by those skilled in the art of molecular biology as including T3 and T7 promoters that flank the cloning site, which allow expression of the inserted gene sequence. Appendix C shows the key structural features of this vector. The entire MCOLN1 open reading frame is present in IMAGE CLONE 2517653.

13. These documents verify our reduction to practice in the United States of America, prior to Aug. 17, 1999, of the subject matter of claims 1, 5-7, 33-35, and 39.

14. We further declare that all statements made herein of our own knowledge are true, and that all statements made on information and belief are believed to be true. We further declare that these statements are made with the knowledge that the willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the instant application or of any patent issued thereupon.

Respectfully submitted,

11/28/2004
DATE


Ehud Goldin

DATE

Susan A. Slaughaupt

DATE

Mei Sun

DATE

James S. Acierno, Jr

Respectfully submitted,

DATE

12-13-04

DATE

Ehud Goldin



Susan A. Slaughaupt

DATE

Mei Sun

DATE

James S. Acierno, Jr

Respectfully submitted,

DATE

Ehud Goldin

DATE

Susan A. Slaughaupt

DATE

Mei Sun

DATE

James S. Acierno, Jr

Respectfully submitted,

DATE

Ehud Goldin

DATE

Susan A. Slaughaupt

DATE

Mei Sun

12/19/04

DATE

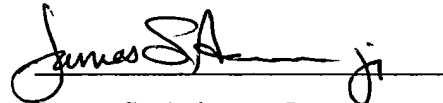

James S. Acierno, Jr

EXHIBIT A • PAGE 1

IDT[®]

Integrated DNA Technologies, Inc.

Oligonucleotide Specification Sheet

1740 Commercial Park
Coram, MA 02241
Phone: 800-328-2661
Fax: 508-626-8444
E-Mail: orders@idtdna.com
<http://www.idtdna.com>

Customer Information

Susan Slaughaupt
Harvard Institute of Human Genetics
Massachusetts General Hospital-Boston
77 Avenue Louis Pasteur HIM Bldg. Rm. 422
Boston, MA 02115
6174327025

Order Information

Order Date :
Customer # : 19479
P.O. # : 0000085288

Sales order # : 148396
Reference #: 624757

Oligonucleotide Information

Reference # : 624757
Purification : Standard Purification
Sequence Name : sts-T66288-1

Product : DNA Oligo Sample
Unit Size : 100 nmole
Bases : 20

Sequence : 5'-GGC AGT CAG GTC GAA TCA AT-3'

$$\begin{array}{r} 10 \times 7 = 70 \\ 10 \times 2 = 20 \\ \hline 90 \end{array}$$

Molecular Weight : 7,572.00
GC Content : 50.0 %
Tm (50mM NaCl) : 51.44 °C

Amount of Oligo

21.8 = 95.01 = 0.72
OD₂₆₀ nanomoles mg

Printed 6/3/99

1569

LABELS - PEEL HERE

624757 Integrated DNA Tech
S. Slaughaupt 06/03/99
sts-T66288-1
5'-GGC AGT CAG GTC GAA TCA AT-3'
Tm = 51.44 °C, MW = 7572
21.80 OD₂₆₀ = 95.01 nmol = 0.72 mg

624757 Integrated DNA Tech
S. Slaughaupt 06/03/99
sts-T66288-1
5'-GGC AGT CAG GTC GAA TCA AT-3'
Tm = 51.44 °C, MW = 7572
21.80 OD₂₆₀ = 95.01 nmol = 0.72 mg

Samples Statistically Tested

Q.C. Approved By:

PLEASE READ BEFORE OPENING TUBES

- * Store at -20°C. If the oligo is to be used on multiple occasions, resuspend in water or tris-EDTA buffer, divide into smaller aliquots, lyophilize, and store at -20°C.
- * Contents may appear as either a translucent film or a white powder. This variance does not affect the quality of the oligo.
- * Please centrifuge tubes prior to opening. Some of the product may have been dislodged during shipping.
- * Calculations are made using 1 OD₂₆₀ = 33 µg / mL

Sold for research purposes only.

EXHIBIT A

AGE 2

Integrated DNA Technologies, Inc.

Oligonucleotide Specification Sheet

17510 Commercial Park
Coral Gables, FL 33156
Tel: 800-328-2881
Fax: 305-628-8444
E-mail: orders@idtdna.com
www.idtdna.com

Customer Information

Susan Slaughaupt
Harvard Institute of Human Genetics
Massachusetts General Hospital-Boston
77 Avenue Louis Pasteur HIM Bldg. Rm. 422
Boston, MA 02115
6174327025

Order Information

Order Date :
Customer #: 19479
P.O. #: 0000085288

Sales order #: 148396
Reference #: 624758

Oligonucleotide Information

Reference #: 624758
Purification: Standard Purification
Sequence Name: sts-T66288-R

Product: DNA Oligo Sample
Unit Size: 100 nmole
Bases: 18

Sequence: 5'- AGC TGC AGG GGT ACA TCG -3'

$$\frac{11 \times 4 = 44}{7 \times 2 = 14} = \frac{44}{58}$$

Molecular Weight : 6,754.00
GC Content : 61.1 %
Tm (50mM NaCl) : 51.11 °C

Amount of Oligo
15.5 = 75.73 = 0.51
OD₂₆₀ nanomoles mg

Printed 6/9/99

LABELS - PEEL HERE

624758 Integrated DNA Tech
S. Slaughaupt 06/09/99
sts-T66288-R
5'-AGC TGC AGG GGT ACA TCG-3'
Tm = 51.11 °C, MW = 6754
18.50 OD₂₆₀ = 75.73 nmol = 0.51 mg

624758 Integrated DNA Tech
S. Slaughaupt 06/09/99
sts-T66288-R
5'-AGC TGC AGG GGT ACA TCG-3'
Tm = 51.11 °C, MW = 6754
18.50 OD₂₆₀ = 75.73 nmol = 0.51 mg

Samples Statistically Tested
Q.C. Approved By:

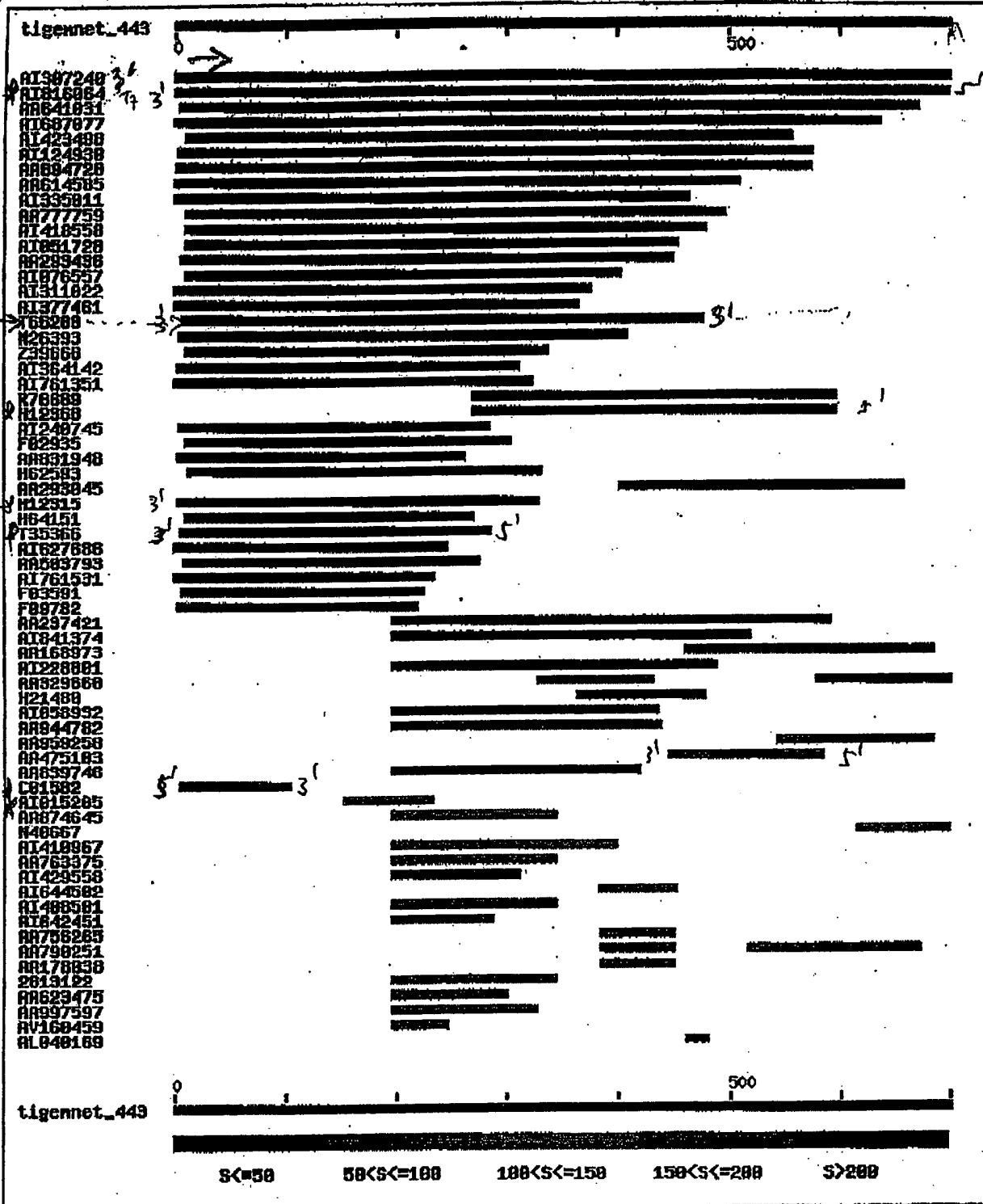
PLEASE READ BEFORE OPENING TUBES

- Store at -20°C. If the oligo is to be used on multiple occasions, resuspend in water or tri-EDTA buffer, divide into smaller aliquots, lyophilize, and store at -20°C.
- Contents may appear as either a translucent film or a white powder. This variance does not affect the quality of the oligo.
- Please centrifuge tubes prior to opening. Some of the product may have been dislodged during shipping.
- Calculations are made using 1 OD₂₆₀ = 33 µg/mL.

Sold for research purposes only.

EXHIBIT B

313 44914



SEQ ID NO: 2

<400> 2

----- sts-T66288-f

----- sts-T66288-r

agatcagctg atgccggagg gtttgaagcc gcgccgcgag ggagcgaggt cgcagtgaca 60
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ccagcatgac agccccggcg ggtccgcgcg gctcagagac cgagcggctt ctgacccccca 180
acccccggta tgcgacccag gcggggcctt caccggcccc tccgacaccc ccagaagagg 240
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cggcctgcag cttctctgc tgcctcggaa gggacccctc ggaggagcat tgcctgctgg 1860
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gaggagggcc tggaccttctc gtgtcggacc cttggggggcg gggagactgg gtggggaggg 2040
tgttgaataa a. 2051

APPENDIX B



The I.M.A.G.E. Consortium

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Result Number	CLONE ID	ROW POS	COL POS	PLATE	GB ACCNUM	SEQ LENGTH	GB DATE CREATED	DATE MODIFIED	CDNA LIBR ID	SPECIES	TISSUE TYPE	VECTOR NAME
1	2517653	1	6	6268	AI815981	448	Jul 09 1999 12:00AM	Apr 17 2003 05:06PM	1341	human	brain/CNS	pBluescript SK+
2	2517653	1	6	6268	AI816064	706	Jul 09 1999 12:00AM	Apr 17 2003 05:06PM	1341	human	brain/CNS	pBluescript SK+

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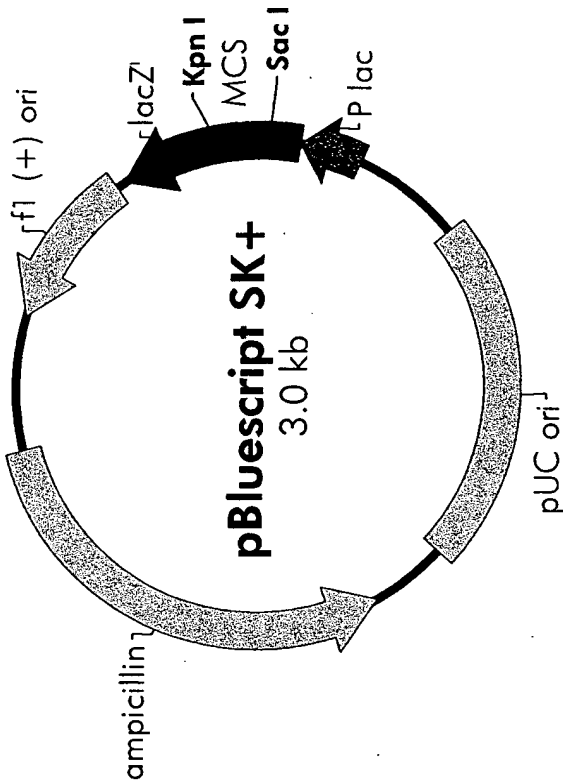
BBRP home page



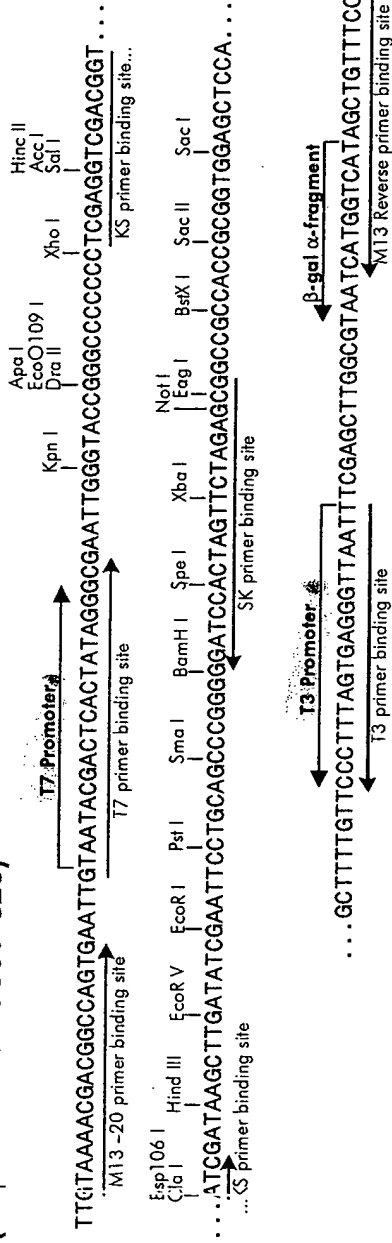
LLNL Programs, Projects, Centers and Consortia

APPENDIX C

f1 (+) origin 138-444
 β-galactosidase α-fragment 463-816
 multiple cloning site 653-760
 lac promoter 817-938
 pUC origin 1158-1825
 ampicillin resistance (bla) ORF 1976-2833



pBluescript SK (+/-) Multiple Cloning Site Region (sequence shown 601-826)



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